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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,557	06/12/2002	Olga Bandman	PF-0693 USN	5013

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,557	BANDMAN ET AL.	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *7,9,12-14 and 16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,10,11 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 7, 9, 12-14, 16-23 have been previously withdraw from consideration. Amended claims 1-4, 10 (10/25/04) and original claims 5, 8, 11, 15 are under consideration by the Examiner.

2. Receipt of applicant's arguments and amendments filed on 10/25/2004 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 10/25/2004:

(i) the objection to claim 3;

(ii) the rejection of claim 6 under 35 U.S.C. 112, first paragraph, scope of enablement;

(iii) the rejection of claims 1-6, 8, 10-11, 15 under 35 U.S.C. § 112, second paragraph; and

(iv) the rejection of claims 1, 3, 5-6, 8, 15 under 35 U.S.C. 102(b) as being anticipated by Ntwasa et al (1994).

4. Applicant's arguments filed on 10/25/04 have been fully considered and were persuasive in part. The remaining issues are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101, 112 first paragraph

6. Claims 1-6, 8, 10-11, 15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

This rejection is maintained for reasons of record set forth at pages 4-7 of the previous Office action (7/23/2004).

Applicants argue that the specification broadly defines the utility of the invention reciting its use for diagnosis, treatment, or prevention of cell proliferation, immune, reproductive, neuronal and genetic disorders and that Table 3 shows that SEQ ID NO:34 is associated with cancer, inflammation and cell proliferation (see page 25 and Table 3). Applicants also argue that Jang et al (2001), which is a post-filing date publication, discloses a peptide LRR-1 with 100% sequence identity to SEQ ID NO:9, said LRR-1 associates with 4-1BB (a member of the TNF receptor family). Therefore, Applicants conclude that since interactions of 4-1BB with its ligand increases IL2 production and proliferation and survival of T cells, this teaching in the reference supports the teaching in the instant specification teaching diagnostics and treatment of cancer. However, contrary to Applicants arguments, the asserted utility argued by applicants is credible because we now know that SEQ ID NO:9 is identical to LRR-1 which associates with 4-1BB which is a member of the TNF receptor family. But, the instant specification fails do disclose this fact. The teachings of Jang et al are not disclosed in the instant specification. Therefore, the utility broadly defined in the instant specification, is not specific or substantial.

In light of the disparate broadly defined utilities disclosed in the instant specification, MPEP §2145 clearly states that attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection (MPEP § 2129 and §2144.03). Applicants are reminded that "Argument of counsel cannot take the place of evidence lacking in the record" (*In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974)).

In the instant case, Applicants are asserting that the instant protein of SEQ ID NO:9 associates with 4-1BB, while no data, information, or teaching supports this observation in the

instant Specification {see *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Claim Rejections - 35 USC § 112, first paragraph, written description

7. Claims 1-6, 8, 10-11, 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons of record set forth at pages 8-11 of the previous Office action (7/23/2004).

Applicants argue that with respect to claim 11 which recites "comprising at least 60 contiguous nucleotides", the specification does describe common attributes and characteristics that identify members of the genus as seen in Table 2 which includes "signature sequence" information which shows the leucine-rich repeats (LRR) in SEQ ID NO:34. Applicants argue that LRR are known to be involved in protein-protein interactions such as signal transduction and cellular adhesion. However, contrary to Applicants arguments, with respect to both the "comprising at least 60 contiguous nucleotides" and "95% sequence identity limitation", the instant claims are drawn to a genus of polypeptides that is defined by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim

that is sufficiently disclosed is a partial structure in the form of a recitation of "percent identity" and "60 contiguous nucleotides". The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is a polypeptide comprising SEQ ID NO: 9. No active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 9, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

7. Claims 1, 3, 5-6, 8, 10-11, 15 are rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:9, does not reasonably provide enablement for an isolated polynucleotide "...having at least 95% sequence identity to SEQ ID NO:34" or an isolated polypeptide "...having at least 95% identity to SEQ ID NO:9". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 14-15 of the previous Office action (7/23/2004).

Applicants argue that the ability to manipulate polynucleotide libraries to obtain new polynucleotides is routine and some experimentation is permissible. However, contrary to Applicants arguments, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This position is consistent with the decisions in In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and

Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., 13 USPQ2d, 1737 (1990), and In re Wands, 8USPQ2d, 1400 (CAFC 1988) (which has been cited by Applicants. If Applicants will kindly review page 1404 of In re Wands, they will find that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims. Applicants arguments that the standard is that of mutating a subject protein (95% sequence identity) and testing to see if it retains the desired biological activity is a position that has been routinely dismissed by the courts, as shown by the decisions cited above.

Further, In re Wands determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally-occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a protein whose amino acid sequence deviates from SEQ ID NO:9 by as much as 5%. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed naturally-occurring protein sequence, which are required for functional and structural integrity of the protein. It is this additional characterization of the disclosed protein that is required in order to

obtain the functional and structural data needed to permit one to produce a protein, which meets the structural requirement of the instant claims that constitutes undue experimentation.

Furthermore, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph, in a recent CAFC decision, Genentech, Inc. v. Novo. Nordisk, 42 USPQ2d, 100 (CAFC 1997), in which the decisions in In re Fisher, Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., and In re Wands were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the Court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not, without actually making and testing them, then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that any protein having 95% amino acid sequence identity to the disclosed protein will more likely than not perform in the manner disclosed and the instant specification does not provide the guidance needed to predictably alter the amino acid sequences with any reasonable expectation that the resulting protein will be the desirable protein.

Applicants argue that the teachings of the present application, especially when taken together with the knowledge of one of ordinary skill in the pertinent art, provide an enabling disclosure. However, contrary to Applicants arguments, the cited portion of the specification (Tables 2-3) is not adequate guidance as to the nature of the protein analogues or variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Therefore Applicants have not presented enablement commensurate in scope with the claims.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
November 9, 2004